REMARKS

Status of Claims and Amendment

Claims 1, 20, and 36 have been amended. Claims 1-6, 13 and 16-39 are all the claims pending in the application. Claims 14 and 15 have been canceled without prejudice. Claims 7-12 were previously canceled without prejudice. Claims 13, 17-19, 21-35, 38, and 39 are withdrawn from consideration as being directed to a non-elected invention.

Claim 1 has been amended to incorporate the limitations of claims 14 and 15.

Claim 20 has been amended to clarify that the fusion protein molecule of the binding protein and the antibody Fc region form a dimer. Support for the amendment to claim 20 may be found the specification, for instance, at page 16, line 30 to page 17, line 13.

Claim 36 has been amended to replace "the antibody" with "the fusion protein". Support for the amendment to claim 20 may be found the specification, for instance, at page 14, lines 22-32 and page 46, line 24 to page 52, line 8.

The specification at page 23, lines 1-15 has been amended to indicate that the biological deposits were made under the Budapest Treaty in compliance with 37 C.F.R. 1.804(a) and 1.809(d).[1] Applicants note that the deposited biological material fully meets the requirements of 37 C.F.R. §§1.802(a) and (b), §1.803(a), and §1.804(a), M.P.E.P. §2406.01, and §112, first paragraph, for enablement.

No new matter is added.

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[1] In addition, Applicants submit herewith copies of the original biological receipt of deposits for FERM BP 8499, FERM BP-8500, and FERM BP-8503, the English translation of these original biological receipt of deposits, and a Statement of Availability for FERM BP 8499, FERM BP-8500, and FERM BP-8503.

Claim of Priority

Applicants note the Examiner has not acknowledged Applicants' claim of foreign priority to JP 2003-350158, as well as receipt of a certified copy of the foreign priority document which was received from the International Bureau on April 10, 2006.

Applicants respectfully request the Examiner indicate acknowledgement of Applicants' claim of priority as well as receipt of the priority document in the next Office Communication.

Information Disclosure Statements

Applicants thank the Examiner for acknowledgement and consideration of the Information Disclosure Statements filed April 10, 2006, October 15, 2007, and December 14, 2007, by returning signed and initialed copies of the PTO Forms SB/08 submitted therewith.

Response to Claim Objections

Claim 20 is objected to because the recitation "wherein the fusion protein composition is a dimer" is unclear whether the fusion protein is a dimer or the composition is a dimer.

Applicants note that one of ordinary skill in the art would understand from reading the specification, for instance, at page 16, line 30 to page 17, line 13, that a dimer is formed between the fusion protein molecule of a binding protein and antibody Fc region in the fusion protein composition. Nevertheless, and solely to advance prosecution of the present application, claim 20 has been amended to recite that "the fusion protein molecule of the binding protein and the antibody Fc region form a dimer".

Withdrawal of the grounds of objection is respectfully requested.

Response to Rejection under 35 U.S.C. § 112, for Indefiniteness

Claim 36 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

Specifically, the limitation "purifying the antibody from the culture" in line 4 is asserted to have insufficient antecedent basis since "fusion protein" and not "the antibody" is recited.

In response, Applicants note that based upon the disclosure at page 14, lines 22-32 and page 46, line 24 to page 52, line 8, one of ordinary skill in the art would understand this is a clerical error. Accordingly, claim 36 has been amended to replace "the antibody" with "the fusion protein".

Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Response to Rejection under 35 U.S.C. § 112, for Enablement

Claim 16 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

Specifically, the Office Action asserts that claim 16 is drawn to a fusion protein produced by FERM BP-8499, and the hybridoma FERM BP-8499 is required to practice the claimed invention. Although the Office Action notes that FERM BP-8499 is deposited with the International Patent Organism Depositary, National Institute of Advanced Industrial Science and Technology, Central 6, 1, Higashi 1-chome, Tsukuba-shi, Ibaraki, Japan, on Sep. 30, 2003, before the filing of the present application, which is an acceptable international depository

authority under 37 C.F.R. § 1.803 (see MPEP 2405), it is unclear whether the deposit was made under the terms of the Budapest Treaty.

The Office Action appears to assert that if the deposit is made under the Budapest Treaty, then a Statement of Availability needs to be filed.

Otherwise, if the deposit was not made under the Budapest treaty, then an affidavit or declaration should be submitted with an assurance that the deposit has been made at an acceptable depository and that the criteria set forth in 37 C.F.R. § 1.801-1.809, have been met.

In response, Applicants note that a biological deposit was made for transformed CHO cell lines designated as FERM BP-8499, FERM BP-8500, and FEMR BP-8503 as disclosed at page 23, lines 1-15 of the specification. In addition, Applicants submit herewith copies of the original biological receipt of deposits for FERM BP 8499, FERM BP-8500, and FERM BP-8503, made according to the Budapest Treaty, the English translation of these original biological receipt of deposits, and a Statement of Availability.

Thus, the deposited biological material fully meets the requirements of 37 C.F.R. §§1.802(a) and (b), §1.803(a), and §1.804(a), M.P.E.P. §2406.01, and §112, first paragraph requirement for enablement.

Withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Response to Rejection of Claims 1-6, 20, 36 and 37 Under 35 U.S.C. § 102

Claims 1-6, 20, 36, and 37 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kanda *et al.* (U.S. Patent Publication No. 2003/0115614).

Kanda is asserted to teach (1) an antibody or a fusion protein composition and a medicament thereof comprising an antibody with an Fc region wherein the Fc region comprises complex type N-glycoside-linked sugar chains having a structure in which fucose is not bound to N-acetylglucosamine in the reducing end in the sugar chain; (2) an Fc region can be of human IgG1 subclass comprising a hinge region, a CH2 and a CH3 region; (3) the fusion protein can be a dimer; (4) the fusion protein exhibits enhanced effector function including antibody-dependent cell mediated cytotoxicity (ADCC); and (5) that the fusion protein or antibody can be produced by host cells that are transformed with DNA encoding the fusion protein or antibody followed by purifying the protein or antibody from the culture medium.

Applicants assert that the presently claimed invention is not inherently or explicitly disclosed by Kanda. In this respect, Applicants note that claim 1 has been amended to incorporate the limitations of claim 14, which is not rejected.

Withdrawal of the rejection under 35 U.S.C. § 102(b), is respectfully requested.

Response To Rejections Under 35 U.S.C. § 103(a)

Claims 1, 14, and 15 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Presta (U.S. Patent Publication No. 2003/0157108) in view of Jacobs *et al.* (U.S. Patent No. 5,605,690).

Presta is asserted for teaching immunoadhesin, e.g., soluble TNFR combined with IgG Fc region, as a therapeutic to treat human diseases by blocking ligand receptor interaction and recruiting the immune system effector cells to kill target cells, as well as glycoproteins in which the Fc region comprises a complex sugar structure that lacks fucose. However, the Office Action acknowledges that Presta does not teach a soluble TNFR II comprising SEQ ID NO:64.

Jacobs is asserted for teaching a dimerized soluble TNF receptor conjugated with human IgG1 Fc region that is allegedly 100% identical in amino acid sequence to the claimed SEQ ID NO:64.

Thus, absent evidence to the contrary, the Office Action concludes that it would have been obvious to one of skill in the art at the time of the invention to combine the teachings of Presta with Jacobs to make a soluble TNFRII-Fc protein with N-glycan sugar structures in which fucose is not bound to N-acetylglucosamine. The Office Action asserts that the claimed elements are known in the art, and a skilled artisan would have been motivated to modifying Presta with Jacobs with a reasonable expectation of success of obtaining the claimed invention because the combination would have yielded predictable results.

Initially, Applicants note that the Office Action has failed to establish a *prima facie* case of obviousness for at least the following reasons.

First, Presta and Jacobs, alone or in combination, fail to teach each and every element of the claimed invention to establish a *prima facie* case of obviousness.

Presta does not disclose, either expressly or inherently, antibody molecules wherein 100% of the antibody molecules do not contain sugar chains with a fucose bound to the N-acetylglucosamine. Rather, Presta is directed to glycoprotein production in Lec13 cells, which cells exhibit a *reduction in*, but not absence of, GDP-mannose 4,6-dehydratase (GMD) activity. Specifically, as shown in Figure 1B and Table 1, Lec13 cells are unable to produce antibodies wherein 100% of the antibody molecules do not contain sugar chains with a fucose bound to the N-acetylglucosamine, at any time during culture. To the contrary, due to the low level of GMD activity in Lec13 cells, this results in the production of a population of antibody molecules

containing sugar chains with a fucose bound to the N-acetylglucosamine. Accordingly, Presta fails to teach or suggest antibody molecules wherein 100% of the antibody molecules do not contain sugar chains with a fucose bound to the N-acetylglucosamine. Also, as admitted by the Office Action, although Presta teaches a soluble TNF receptor, Presta does not teach the claimed amino acid sequence of SEQ ID NO:64.

Furthermore, even if one of ordinary skill in the art was somehow motivated to combine Presta and Jacobs, which one would not be, the combination of Presta and Jacobs would still not result in the presently claimed invention because neither Presta nor Jacobs teaches or suggests antibody molecules wherein 100% of the antibody molecules do not contain sugar chains with a fucose bound to the N-acetylglucosamine.

Thus, neither Presta or Jacobs, alone or in combination would have rendered the presently claimed invention obvious to one of ordinary skill in the art at the time the invention was made.

Nevertheless, and solely to advance prosecution of the present application, claim 1 has been amended to clarify that the claimed fusion proteins comprise an antibody Fc region having complex type N-glycoside-linked sugar chains, wherein the complex type N-glycoside-linked sugar chains have a structure that <u>does not contain fucose</u> bound to N-acetylglucosamine and that the soluble receptor is a soluble TNF (tumor necrosis factor) receptor II comprising the amino acid sequence of SEQ ID NO: 64.

Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a), is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The U.S. Patent and Trademark Office is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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